CLAIMS

1. A method for detecting in a sample the presence of a nucleic acid Q' whose nucleotide sequence differs from a nucleic acid Q in at least one position A, the method comprising the steps of

a) combining nucleic acids present in the sample with an appropriate amount of nucleoside triphosphates, an agent for polymerisation of the nucleoside triphosphates and at least one diagnostic oligonucleotide containing at position A a nucleotide which is capable of hybridizing to the nucleotide at position A of nucleic acid Q' but not to a nucleotide at position A of nucleic acid Q under hybridisation conditions, the at least one diagnostic oligonucleotide containing at least one LNA,

b) extending any oligonucleotides which hybridize to the nucleic acids present in the sample to form extension products, wherein said nucleic acids are used as templates,

c) detecting any nucleic acids formed in step b) and thereby the presence of nucleic acid Q' in the sample.

2. A method for detecting in a sample the presence of a nucleic acid Q' whose nucleotide sequence differs from a nucleic acid Q in at least one position A, the method comprising the steps of

a) combining nucleic acids present in the sample with an appropriate amount of nucleoside triphosphates, an agent for polymerisation of the nucleoside triphosphates and at least one diagnostic oligonucleotide containing at position A a nucleotide which is capable of hybridizing to the nucleotide at position A of nucleic acid Q' but not to a nucleotide at position A of nucleic acid Q under hybridisation conditions, the at least one diagnostic oligonucleotide containing at least one LNA,

b) extending any oligonucleotides which hybridize to the nucleic acids present in the sample to form extension products, wherein said nucleic acids are used as

templates,

c) after the formation of extension products treating the reaction mixture under denaturing conditions to separate the extension products from the template,

d) hybridising in the presence of an appropriate amount of nucleoside triphosphates and an agent for polymerisation of the nucleoside triphosphates the single stranded nucleic acids of step c) with at least one diagnostic oligonucleotide containing at position A a nucleotide which is capable of hybridizing to the nucleotide at position A of nucleic acid Q' but not to a nucleotide at position A of nucleic acid Q under hybridisation conditions, the at least one diagnostic oligonucleotide containing at least one LNA,

e) repeating steps c) and d) a sufficient number of times to result in a detectable amount of extension products,

f) detecting the extension products formed.

3. A method for detecting in a sample the presence of a nucleic acid Q' whose nucleotide sequence differs from a nucleic acid Q in at least one position A, the method comprising the steps of

a) combining the nucleic acids with an appropriate amount of nucleoside triphosphates, an agent for polymerisation of the nucleoside triphosphates, at least one downstream oligonucleotide and at least one diagnostic oligonucleotide containing at position A a nucleotide which is capable of hybridizing to the nucleotide at position A of nucleic acid Q' but not to a nucleotide at position A of nucleic acid Q under hybridisation conditions, the at least one diagnostic oligonucleotide containing at least one LNA,

b) extending any oligonucleotides which hybridize to the nucleic acids to form extension products, wherein said nucleic acids are used as templates,

c) after the formation of extension products treating the reaction mixture under denaturing conditions to separate the extension products from the template,

d) hybridising in the presence of an appropriate amount of nucleoside triphosphates and an agent for polymerisation of the nucleoside triphosphates the single stranded nucleic acids from step c) with at least one downstream oligonucleotide and at least one diagnostic oligonucleotide containing at position A a nucleotide which is capable of hybridizing to the nucleotide at position A of nucleic acid Q' but not to a nucleotide at position A of nucleic acid Q under hybridisation conditions, the at least one diagnostic oligonucleotide containing at least one LNA,

e) repeating steps c) and d) a sufficient number of times to result in a detectable amount of extension products,

f) detecting the extension products formed.

4. A method for detecting target nucleic acids whose nucleotide sequences differ from one another in at least one position A, the method comprising the steps of

a) combining the nucleic acids with an appropriate amount of nucleoside triphosphates, an agent for polymerisation of the nucleoside triphosphates and at least one set of diagnostic oligonucleotides under hybridisation conditions, the at least one set of diagnostic oligonucleotides having nucleotide sequences which differ from one another in at least one position A and contain at least one LNA,

b) extending any oligonucleotides which hybridize to the nucleic acids to form extension products, wherein said nucleic acids are used as templates,

c) detecting the nucleic acids formed in step b).

5. A method for detecting target nucleic acids whose nucleotide sequences differ from one another in at least one position A, the method comprising the steps of

a) combining the nucleic acids with an appropriate amount of nucleoside triphosphates, an agent for polymerisation of the nucleoside triphosphates and at least

one set of diagnostic oligonucleotides under hybridisation conditions, the at least one set of diagnostic oligonucleotides having nucleotide sequences which differ from one another in at least one position A and contain at least one LNA,

b) extending any oligonucleotides which hybridize to the nucleic acids to form extension products, wherein said nucleic acids are used as templates,

c) after the formation of extension products treating the reaction mixture under denaturing conditions to separate the extension products from the template,

d) hybridising in the presence of an appropriate amount of nucleoside triphosphates and an agent for polymerisation of the nucleoside triphosphates the single stranded nucleic acids from step c) with at least one set of diagnostic oligonucleotides whose nucleotide sequences differ from one another in at least one position A to synthesise further extension products,

e) repeating steps c) and d) a sufficient number of times to result in a detectable amount of extension products,

f) detecting the extension products formed.

6. A method for detecting target nucleic acids whose nucleotide sequences differ from one another in at least one position A, the method comprising the steps of

a) combining the nucleic acids with an appropriate amount of nucleoside triphosphates, an agent for polymerisation of the nucleoside triphosphates, at least one downstream oligonucleotide and at least one set of diagnostic oligonucleotides under hybridisation conditions, the at least one set of diagnostic oligonucleotides having nucleotide sequences which differ from one another in at least one position A and contain at least one LNA,

b) extending any oligonucleotides which hybridize to the nucleic acids to form extension products, wherein said nucleic acids are used as templates,

c) after the formation of extension products treating the reaction mixture under denaturing conditions to separate the extension products from the template,

d) hybridising in the presence of an appropriate amount of nucleoside triphosphates and an agent for polymerisation of the nucleoside triphosphates the single stranded nucleic acids step c) with at least one downstream oligonucleotide and at least one set of diagnostic oligonucleotides being oligonucleotides whose nucleotide sequences differ from one another in at least one position A to synthesise further extension products,

e) repeating steps c) and d) a sufficient number of times to result in a detectable amount of extension products,

f) detecting the extension products formed.

7. A method for detecting target nucleic acids whose nucleotide sequences differ from one another in at least one position A, the method comprising the steps of

a) combining the target nucleic acids with an appropriate amount of nucleoside triphosphates, at least two oligonucleotides wherein at least one of said oligonucleotides is a diagnostic oligonucleotide and an agent for ligation of the oligonucleotides under hybridisation conditions, the at least one diagnostic oligonucleotide being an oligonucleotide containing at position A a nucleotide which is complementary to the nucleotide found at position A of the target nucleic acid to be detected, said diagnostic oligonucleotide contains at least one LNA,

b) ligating any oligonucleotides which hybridize to the nucleic acids at adjacent positions to form ligation products, wherein said nucleic acids are used as templates,

c) detecting the nucleic acids formed in step b).

8. A method for detecting target nucleic acids whose nucleotide sequences differ from one another in at least one position A, the method comprising the steps of

a) combining the target nucleic acids with an appropriate amount of nucleoside triphosphates, at least two oligonucleotides wherein at least one of said oligonucleotides is a diagnostic oligonucleotide and an agent for ligation of the oligonucleotides under hybridisation conditions, the at least one diagnostic oligonucleotide being an oligonucleotide containing at position A a nucleotide which is complementary to the nucleotide found at position A of the target nucleic acid to be detected, said diagnostic oligonucleotide contains at least one LNA,

b) ligating any oligonucleotides which hybridize to the nucleic acids at adjacent positions to form ligation products, wherein said nucleic acids are used as templates,

c) treating the reaction mixture under denaturing conditions to separate the ligation products from the template after the ligation,

d) hybridising in the presence of an appropriate amount of nucleoside triphosphates and an agent for ligation of the oligonucleotides under hybridisation conditions the single stranded nucleic acids from step c) with at least one oligonucleotide being complementary to the ligation product from step b) and at least two oligonucleotides the at least one diagnostic oligonucleotide being an oligonucleotide containing at position A a nucleotide which is complementary to the nucleotide found at position A of the target nucleic acid to be detected, said diagnostic oligonucleotide contains at least one LNA,

e) repeating steps c) and d) a sufficient number of times to result in a detectable amount of ligation products,

f) detecting the ligation products formed.

9. A method according to any of the preceding claims, wherein the at least one position A of the diagnostic oligonucleotide sequence is complementary to position A of the nucleic acid sequence to be detected but not to position A of the other nucleic acid sequences.

10. A method according to any of the preceding claims, wherein the nucleotide at the at least one position A in the diagnostic oligonucleotide is a LNA.

11. A method according to any of claims 1-10, wherein the diagnostic oligonucleotide has the general formula

a) $5'\text{-}Nu_a(Nu_bLNA_c)_mNu_dA_eNu_f\text{ -}3'$

where A is a LNA in position A in which the variant nucleic acid sequences of the target nucleic acids differs from one another; LNA is a LNA; Nu is a monomer selected from the group consisting of any nucleotides other than LNA capable of forming specific base-pairs with the variant nucleic acids; a, b, c, d and f are integers between 0 and 30, m is an integer between 1 and 8 and e is an integer between 1 and 6 with the proviso that the sum of a, b, c, d, e and f is at least 5.

12. A method according to claim 11, wherein a=10, b=0, c=4, d=8, e=1, f=0, m=0 in the general formula a.

13. A method according to claim 11, wherein a=0, b=1, c=1, d=8, e=1, f=0, m=5 in the general formula a.

14. A method according to claim 11, wherein a=10-30, b=0, c=0, d=0, e=1-4, f=1-8, m=0 in the general formula a.

15. A method according to claim 11, wherein a=10-30, b=0, c=0, d=0, e=1-4, f=1, m=0 in the general formula a.

16. A method according to claim 11, wherein a=10-30, b=0, c=0, d=0, e=1-4, f=0, m=0 in the general formula a.

17. A method according to claim 11, wherein a=10-30, b=0, c=0, d=0, e=1, f=0, m=0 in the general formula a.

18. A method according to claim 11, wherein a=10, b=0, c=0, d=0, e=4, f=8, m=0 in the general formula a.

19. A method according to claim 11, wherein a=24, b=0, c=0, d=0, e=1, f=0, m=0 in the general formula a.

20. A method according to any of the preceding claims, wherein the at least one diagnostic oligonucleotide is covalently attached to a solid support.

21. A method according to claim 20, wherein the different diagnostic oligonucleotides are spotted in an array format on the solid surface.

22. A method according to any of claims 1-19, wherein the different downstream oligonucleotides are spotted in an array format on the solid surface.

23. A method according to any of claims 20-22, wherein the attachment is performed by the anthraquinone photochemistry.

24. A method according to any of claims 1-21, wherein the at least one diagnostic oligonucleotide is labelled with a detectable group.

25. A method according to any of claims 4-21, wherein the at least one first set of diagnostic oligonucleotides is labelled with detectable groups, said detectable groups being different for the different diagnostic oligonucleotides.

26. A method according to claim 25, wherein the individual oligonucleotides in each oligonucleotide set is labelled with detectable groups, said detectable groups being different for the each individual diagnostic oligonucleotide.

27. A method according to any of claims 1-8, wherein said target nucleic acids to be detected originate from a sample of cells, a tissue sample or a tissue extract.

28. A method according to claim 27, wherein the cells are of archae, prokaryotic or eukaryotic origin.

29. A method according to claim 27, wherein the sample of cells is derived from blood, serum, plasma, reticulocytes, lymphocytes, urine, bone marrow tissue, cerebrospinal fluid or any product prepared from blood or lymph.

30. A method according to claim 27, wherein the tissue sample is derived from muscle biopsy, liver biopsy, kidney biopsy, bladder biopsy, bone biopsy, cartilage biopsy, skin biopsy, pancreas biopsy, a biopsy of the intestinal tract, thymus biopsy, mammae biopsy, uterus biopsy, testicular biopsy, eye biopsy or brain biopsy.

31. A method according to any of claims 28-30, wherein said target nucleic acids to be detected are at least one sequence specific for a particular species of organism.

32. A method according to any of claims 28-30, wherein said target nucleic acids to be detected are at least one sequence specific for a particular species, sub-species or strains of organisms.

33. A method according to any of claims 28-30, wherein said target nucleic acids to be detected are at least one sequence specific for a particular species of micro-organisms.

34. A method according to any of claims 28-30, wherein said target nucleic acids to be detected are at least one sequence specific for a particular species, sub-species or strains of micro-organisms.

35. A method according to any of claims 28-30, wherein said target nucleic acids to be detected are at least one sequence specific for a particular infectious agent.

36. A method according to any of claims 28-30, wherein said target nucleic acids to be detected are at least one sequence specific for a particular species, sub-species or strain of infectious agents.

37. A method according to any of claims 28-30, wherein said target nucleic acids to be detected are at least one sequence specific for genes coding for particular proteins involved in inheritable diseases.

38. A method according to any of claims 28-30, wherein said target nucleic acids to be detected are at least one sequence specific for a gene related to a life style disease.

39. A method according to any of claims 28-30, wherein said target nucleic acids to be detected are at least one sequence specific for a particular gene related to cancer.

40. A method according to claim 38, wherein the life style disease is selected from the group consisting of obesity, familial hypercholesterolaemia, atherosclerosis and diabetes.

41. A method according to any of claims 27-40, wherein said target nucleic acids to be detected are alleles.

42. A method according to any of claims 1-6, wherein the agent for polymerization is an enzyme.

43. A method according to claim 42, wherein the agent for polymerization is a DNA polymerase.

44. A method according to claim 43, wherein the agent for polymerization is a thermostable DNA polymerase.

45. A method according claim 44, wherein the thermostable DNA polymerase is selected from the group consisting of Taq, Pfu, Pwo and Tth.

46. A method according to claim 42, wherein the agent for polymerization is a RNA polymerase.

47. A method according to any of claims 7-8, wherein the agent for ligation is an enzyme.

48. A method according to claim 47, wherein the agent for ligation is a ligase.

49. A kit for detecting in a sample the presence of a nucleic acid Q' whose nucleotide sequence differs from a nucleic acid Q in at least one position A, comprising

a) an appropriate amount of nucleoside triphosphates,

b) an agent for polymerisation of the nucleoside triphosphates,

c) at least one diagnostic oligonucleotide containing at position A a nucleotide which is capable of hybridizing to the nucleotide at position A of nucleic acid Q' but not to a nucleotide at position A of nucleic acid Q under hybridisation conditions, the at least one diagnostic oligonucleotide containing at least one LNA

50. A kit for detecting in a sample the presence of a nucleic acid Q' whose nucleotide sequence differs from a nucleic acid Q in at least one position A, comprising

a) an appropriate amount of nucleoside triphosphates,

b) an agent for polymerisation of the nucleoside triphosphates,

c) at least one downstream oligonucleotide,

d) at least one diagnostic oligonucleotide containing at position A a nucleotide which is capable of hybridizing to the nucleotide at position A of nucleic acid Q' but not to a nucleotide at position A of nucleic acid Q under hybridisation conditions, the at least one diagnostic oligonucleotide containing at least one LNA.

51. A kit for detecting target nucleic acids whose nucleotide sequences differ from one another in at least one position A, comprising

a) an appropriate amount of nucleoside triphosphates,

b) an agent for polymerisation of the nucleoside triphosphates,

c) at least one set of diagnostic oligonucleotides having nucleotide sequences which differ from one another in at least one position A and contain at least one LNA.

52. A kit for detecting target nucleic acids whose nucleotide sequences differ from one another in at least one position A, comprising

a) an appropriate amount of nucleoside triphosphates,

b) an agent for polymerisation of the nucleoside triphosphates,

c) at least one downstream oligonucleotide,

d) at least one set of diagnostic oligonucleotides having nucleotide sequences which differ from one another in at least one position A and contain at least one LNA.

53. A kit for detecting target nucleic acids whose nucleotide sequences differ from one another in at least one position A, the kit comprising

a) nucleoside triphosphates,

b) an agent for ligation,

c) at least two oligonucleotides the at least one diagnostic oligonucleotide being an oligonucleotide containing at position A a nucleotide which is complementary to the nucleotide found at position A of the target nucleic acid to be detected, said diagnostic oligonucleotide contains at least one LNA.